Is robot-assisted gait training intensity a determinant of functional recovery early after stroke? A pragmatic observational study of clinical care

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Gait rehabilitation is a critical factor in functional recovery after a stroke. The aim of this pragmatic observational study was to identify the optimal dose and timing of robot-assisted gait training (RAGT) that can lead to a favourable outcome in a sample of subacute stroke survivors. Subacute patients with stroke who underwent a RAGT within a multidisciplinary rehabilitation program were enrolled. A set of clinical (i.e. age, type of stroke and time since stroke) and rehabilitation stay outcomes (length of stay and RAGT number of sessions) were recorded to evaluate their impact on functional outcome measures by functional independence measure (FIM) or functional ambulation category (FAC). We included 236 patients (62.73 ± 11.82 year old); 38.44% were females, and 59.32% were ischaemic stroke patients. Patients that received at least 14 RAGT sessions, had 15.83% more chance to be responders compared to those that receive less sessions (*P* = 0.006). Similarly, younger patients (≤60 years) were more prone to be responders (+15.1%). Lastly, an early rehabilitation (<6 weeks) was found to be more efficient (+21.09%) in determining responsiveness (*P* < 0.001). Becoming newly independent for gait, that refers to a FAC score ≥4, was related with age and RAGT sessions (*P* = 0.001). In conclusion, a younger age (≤60 years), an early rehabilitation (<6 weeks since stroke) and a higher RAGT dose (at least 14 sessions) were related to a favourable outcome in patients with subacute stroke. *International Journal of Rehabilitation Research* 45: 189–194 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

International Journal of Rehabilitation Research 2022, **45**:189–194

Keywords: exercise training, functional independence, robot-assisted gait training, rehabilitation, stroke

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Received 26 November 2021 **Accepted** 18 January 2022

Introduction

Stroke represents one of the most common causes of worldwide long-term disability [1–3]. A large number of survivors have sensory, motor and cognitive impairments responsible for activity limitations and reduced quality of life. The burden of stroke continues to increase globally and more effective management strategies are needed to promote life independence [4]. Gait and mobility impairments represent one of the more documented sequelae [2,5,6]. In the last decades, several new therapeutic approaches, such as robotics, have been introduced in clinical practice to facilitate gait recovery [7,8]. The development of robot-assisted gait devices offered great potential for modern neurorehabilitation based on principles of exercise-related neuroplasticity [9]. So far, robot-assisted gait therapy has been tested successfully in patients with stroke [10–13] and is recommended in addition to multidisciplinary rehabilitation [14,15]. Even though intensity, measured as time spent in rehabilitation activities, seems to be relevant for optimising functional recovery [1,16], scarce evidence is available on the role of robot-assisted gait training (RAGT) dose for functional outcomes. Recently, it has been hypothesised that the dose of RAGT may influence functional recovery in patients who have undergone a multidisciplinary program [17]. The aim of this pragmatic observational study was to identify the optimal dose and timing of RAGT that can lead to a favourable outcome in a sample of subacute stroke survivors. We hypothesized that patients who received a higher RAGT dose at an early stage of recovery will recover better than the others.

Materials and methods

This is a 10-year pragmatic cohort study conducted at the Department of Neuroscience and Rehabilitation at University Hospital of Ferrara, Italy. The study included patients with stroke admitted to an inpatient multidisciplinary programme and received robot-assisted gait therapy (at least seven sessions) between January 2007 and December 2017. Local ethics committee approved the study. Informed consent was obtained from the majority of them, but not from the totality of patients because some of them were no longer attending the rehabilitation clinic. The local ethics committee allows the waiver

DOI: 10.1097/MRR.0000000000000518

of informed consent in case of retrospective study. The STrengthening the Reporting of OBservational studies in Epidemiology guidelines were used to ensure proper reporting of this observational study [18].

The inclusion criteria were: male or female older than 18 years, with a dependent gait due to an ischaemic or haemorrhagic stroke occurred within 6 months from the onset.

Robot-assisted gait training

All patients received RAGT with a robotic exoskeleton (Lokomat, Hocoma, Switzerland) that can guide hip and knee flexion through braces connecting the patient's legs to the machine. It also provides bodyweight support (0–100%) through a harness along with the level of assistance provided by the device. The device can be adjusted according to the patient's needs. Motorised orthoses have a biomechanical role, which is to guide movements at the hips and knees that mimic a physiological gait pattern [19]. Parameters (speed, guidance and bodyweight support) are set according to the functional characteristics of each patient, starting with a 50% of bodyweight reduction and 100% of guidance provided by the robot. Over sessions, adjustments can be made as increments or decrements of 10%. The RAGT sessions last approximately an hour, including patient preparation. The treadmill speed can vary from 0.1 to 3 km/h [14,20].

Multidisciplinary rehabilitation

All patients received a multidisciplinary rehabilitation programme, that is defined according to each individual's needs (conventional motor rehabilitation, occupational therapy, speech therapy and cognitive rehabilitation). At admission, the patient was assessed by a rehabilitation team who defined a specific programme according to the framework of WHO's international classification of functions [21], and at discharge, a clinical evaluation was made to determine the patient's functional improvement [21,22].

Outcomes

A set of demographic, clinical and functional parameters were retrospectively collected from digital medical records: (1) age; (2) sex; (3) time since stroke; (4) functional independence measure (FIM): total score FIM (tFIM), motor subscore FIM (mFIM) and cognitive subscore FIM (cFIM) at admission and discharge and (5) functional ambulation category (FAC) at admission and discharge. In addition, we considered a set of variables related to the rehabilitation training protocol: (1) length of rehabilitation stay (LOS) and (2) number of RAGT sessions.

FIM is a widely used functional performance measure developed specifically for stroke inpatient rehabilitation. It is used to indicate the assistance required by an individual during the performance of 18 motor, self-care, communication and cognitive tasks [23,24]. In our analyses, we identified good responders based on the difference in FIM score at admission and discharge. As minimal clinically important differences (MCID) reported in a previous study [25], we considered a cutoff improvement of 22 points on the global FIM, 17 points for the motor domain and 3 points for the cognitive domain. Moreover, the chance to be newly independent for gait was determined for a FAC score ≥4 at the end of rehabilitation [26–29].

Statistical analysis

The data distribution was verified with the Shapiro–Wilk test. The baseline comparison between the groups was obtained through a chi-square test for categorical variables or an independent samples *t*-test or Mann–Whitney test for continuous variables. Within-group comparison was performed via paired sample *t*-tests or Wilcoxon tests and between-group comparisons for all outcomes were obtained again with independent sample *t*-test or Mann–Whitney test according to data distribution. Multivariate and logistic regression models were employed to determine the impact on the FIM scale variations and on gait independence (FAC score ≥4). When needed, independent variables were opportunely dichotomised as follows: age (≤60 years), length of stay (≥100 days), RAGT sessions (≥14), days since stroke (≤6 weeks), stroke location and hemisphere considering these cutoff as the median values of our sample. A P value <0.05 was considered statistically significant. Data analyses were performed with MedCalc software version 19.2 (MedCalc Software LtD. Ostend, Belgium).

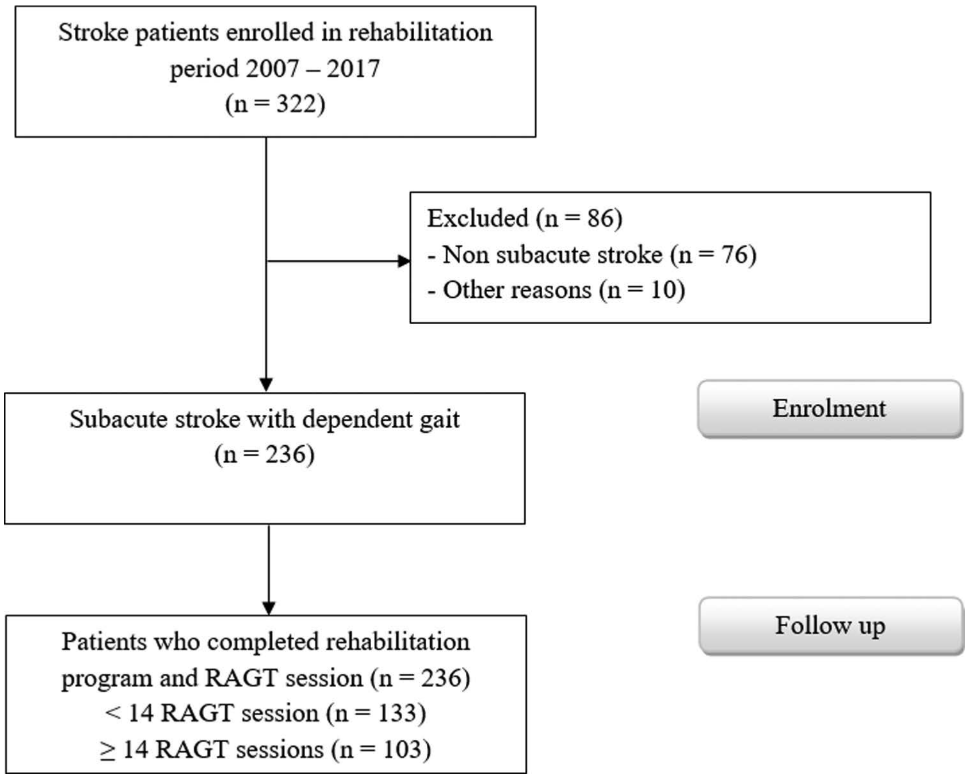
Results

Three hundred and twenty-two patients with stroke who underwent a RAGT during a multidisciplinary rehabilitation programme were assessed. Eighty-six patients were excluded because they did not meet the inclusion criteria. Specifically, we excluded patients with chronic stroke ($n = 76$), and those who interrupted RAGT training for medical reasons ($n = 10$) (Fig. 1).

Sample characteristics

We included 236 participants with a mean age of 62.73 ± 11.82 years old; 91 (38.44%) were female and 145 (61.44%) were male. We highlighted a peak in the distribution for age at 60–70 years that represented 33.4% of the entire population; only 25% of the sample was older than 75 years. Ischaemic strokes were 140 (59.32%) and haemorrhagic were 96 (40.68%). The analysed patients spent an average of 105.49 ± 58.88 days in the inpatient rehabilitation units.

Fig. 1



Study flow-diagram according to STROBE statement. STROBE, STrengthening the Reporting of OBservational studies in Epidemiology.

Table 1 Baseline characteristics of patients under study

	Ischaemic (n=140)	Haemorrhagic (n=96)	Total (n=236)	P value
Age, years	64.22±11.83	60.55±11.52	62.73±11.82	0.019
Male sex, n (%)	87 (62)	58 (60)	145 (61)	0.78
Time since stroke (days)	45.49±38.56	59.22±45.57	51.08±42.01	0.013
Stroke location				
Subcortical	46 (32.90%)	54 (56.20%)	100 (42.40%)	0.42
Cortical-subcortical	63 (45.00%)	30 (31.20%)	93 (39.40%)	<0.001
Cortical	11 (7.90%)	3 (3.10%)	14 (5.90%)	0.033
Brainstem	17 (12.10%)	7 (7.30%)	24 (10.20%)	0.041
Cerebellar	3 (2.10%)	2 (2.10%)	5 (2.10%)	0.65
Side lesion				
Right hemisphere	73 (52.10%)	38 (39.60%)	111 (47.00%)	0.009
Left hemisphere	67 (47.90%)	58 (60.40%)	125 (53.00%)	0.42
LOS (days)	95.05±53.97	120.71±62.60	105.49±58.88	0.001
FAC at admission	0.43±0.73	0.26±0.58	0.36±0.68	0.07
tFIM at admission	48.89±18.10	41.79±19.90	46.00±19.13	0.005
mFIM at admission	25.63±11.81	22.70±11.30	24.44±11.66	0.06
cFIM at admission	23.61±8.81	19.22±10.44	21.82±9.73	0.001

cFIM, cognitive functional independence measure; FAC, functional ambulatory category, LOS, length of stay; mFIM, motor functional independence measure; tFIM: Total functional independence measure.

Ischaemic and haemorrhagic stroke differed for age, time since stroke, LOS, FIM total and cognitive score at admission. Specifically, haemorrhagic patients were younger (P=0.019) received rehabilitation later (P=0.013) with longer LOS (P=0.001) and had a lower FIM score at admission (P=0.005) especially the cognitive domain (P=0.001) (Table 1).

Each participant included in this study completed at least seven RAGT sessions (mean 14.35±7.65), without any adverse event related to the training. After rehabilitation, all patients improved with respect to baseline (P<0.001) without any differences among different types of stroke except for the FIM cognitive domain (P=0.020) (Table 2).

Predictors of functional recovery

Multiple regression models highlighted the predictive effects of some variables on functional gait independence. For total FIM score, a significant model ($R^2=0.26$; $P<0.001$) included age, baseline total FIM score and time since stroke. For motor FIM score, a similar significant model was observed ($R^2=0.25$; $P<0.001$) that included age, baseline motor FIM score and time since stroke. For cognitive FIM score a fitting model was observed ($R^2=0.57$; $P<0.001$) that only included baseline cognitive FIM score and time since stroke.

A logistic regression model predicted the chance to become independent at discharge from rehabilitation [22]. Indeed, a FAC value ≥4 at discharge was related to age [odds ratio (OR), 0.24; 95% confidence interval (CI), 0.12–0.50] and number of RAGT sessions (OR, 2.56; 95% CI, 1.22–5.26) in a significant regression model ($R^2=0.13$; $P<0.001$).

Considering the MCID value described by Beninato *et al.*, [25], we classified our sample as good responders or poor responders and found 74.8% were good responders for total FIM, 74.2% for FIM motor domain and 62.3% for FIM cognitive domain.

Next, we evaluated the differences in the percentage of responders with respect to RAGT dose, age and time since stroke, confirming the positive effects of these factors on functional recovery. Patients that received at least 14 RAGT sessions ($n=103$), were 15.8% more likely to be good responders compared to those who received less sessions ($P=0.006$). Similarly, younger patients (≤60 years) were more prone to be good responders (+15.1%). Lastly, early rehabilitation was found to be more efficient (+21.1%) in determining responsiveness ($P<0.001$). Becoming newly independent for gait, in relation to a FAC score ≥4, was related to age ($P=0.001$) (Table 3).

Discussion

Over the past two decades, RAGT has been introduced in clinical practice as a valuable option to increase training intensity and foster functional recovery in patients with stroke [10,30]. Thus, international guidelines for stroke management recommended its use for patients with severe gait impairments [31,32]. In this pragmatic study, we explored the role of RAGT dose on functional recovery in a large cohort of patients with stroke and dependent walking. Our sample characteristics were similar to other pragmatic studies [20] where patients with stroke that received RAGT were usually younger than the age when stroke more often occurs [33,34] and with a higher percentage of haemorrhagic stroke (40%) compared with the worldwide representation [4]. This can be explained by the fact that haemorrhagic strokes usually are severe with motor and cognitive deficits [35,36]. In our cohort, compared with ischaemic stroke, haemorrhagic patients were younger, started rehabilitation later, had longer rehabilitation length of stay and were more impaired at admission, above all with respect to cognition. Length of stay not only reflects stroke severity and presence of comorbidities but also social and personal factors [13,37]. However, both types of strokes recovered in the same manner, without any differences, as previously reported [38]. Our pragmatic study confirmed several factors that can be determinants for functional recovery after stroke: age, time since stroke and the intensity of training.

In our sample, 37.3% of patients was <60 years old and they recovered significantly more after rehabilitation with a greater chance to be newly gait independent at discharge. These findings confirmed the hypothesis that younger age is related to a better outcome [33,39–42]. Similarly, we found higher functional gains in patients that received RAGT earlier (within 6 weeks). Indeed, a specific time window for spontaneous recovery exists, that can be set within the first 6–12 weeks for gait recovery [22,43,44] when gait robotics are recommended to optimise functional gains [17]. Indeed, a recent update of the Cochrane review has stated that people in the first 3 months after stroke and those who are not able to walk, seem to benefit most from electromechanical-assisted gait training in combination with physiotherapy [14].

Regarding RAGT intensity, defined by the rehabilitation time, in our sample a wide range of training sessions was reported (between 7 and 21). However, a minimum of 14 RAGT sessions have been set to obtain a favourable outcome at discharge. This value is slightly lower than that the 16–18 sessions reported by the Advanced Robotic Therapy Integrated Centers network [20]. The importance of intensity in stroke gait rehabilitation has been elegantly proved by

Table 2 Functional outcomes after rehabilitation

	Ischaemic stroke ($n=140$)			Haemorrhagic stroke ($n=96$)			
	Baseline	Discharge	*P* value	Baseline	Discharge	*P* value	Between-group *P* value
Motor FIM	25.63 ± 11.81	55.37 ± 19.17	<0.001	22.70 ± 11.30	51.01 ± 20.65	<0.001	0.51
Cognitive FIM	23.61 ± 8.81	29.27 ± 5.81	<0.001	19.22 ± 10.44	26.95 ± 8.06	<0.001	0.020
Total FIM	48.89 ± 18.10	84.44 ± 22.17	<0.001	41.79 ± 19.90	77.96 ± 27.02	<0.001	0.81
FAC	0.43 ± 0.73	2.41 ± 1.31	<0.001	0.26 ± 0.58	2.16 ± 1.32	<0.001	0.60

FAC, functional ambulatory category; FIM, functional independence measure.

Table 3 Factors influencing functional recovery after rehabilitation (dose, age and time since stroke)

	≥14 RAGT sessions (*n*=103)	<14 RAGT sessions (*n*=133)	*P* value	<60 Years (*n*=88)	≥ 60 Years (*n*=148)	*P* value	<6 weeks (*n*=138)	≥6 weeks (*n*=98)	*P* value	Total (*n*=236)
tFIM GR, *n* (%)	86 (83.5%)	90 (67.7%)	0.006	74 (84.1%)	102 (68.9%)	0.010	115 (83.3%)	61 (62.2%)	0.001	176 (74.6%)
mFIM GR, *n* (%)	83 (80.6%)	92 (69.2%)	0.048	71 (80.7%)	104 (70.3%)	0.08	114 (82.6%)	61 (62.2%)	0.001	175 (74.2%)
cFIM GR, *n* (%)	75 (72.8%)	79 (59.4%)	0.032	65 (73.9%)	89 (60.1%)	0.033	90 (65.2%)	64 (65.3%)	0.99	154 (65.3%)
FAC ≥4, *n* (%)	15 (14.6%)	30 (22.6%)	0.13	27 (30.7%)	18 (12.2%)	0.001	31 (22.5%)	14 (14.3%)	0.12	45 (19.1%)

cFIM, cognitive functional independence measure; FAC, functional ambulatory category, GR, good responder; mFIM, motor functional independence measure; RAGT, robot-assisted gait training; tFIM: Total functional independence measure.;

Klassen *et al.* [45] that confirmed how higher doses of training determined long-lasting functional effects in subacute stroke patients. However, we should bear in mind that other parameters of training (i.e. velocity, guidance, body-weight support, heart rate and perceived exertion) should be considered when exploring the dose-response relationship of RAGT training. For example, body weight support seems to influence the progression in ambulatory functional categories [46], probably increasing the activity of specific muscles during training [47]. Even gait speed can be considered a training parameter that can affects muscle activity [48]. This pragmatic study was a unique opportunity to open a window on the use of RAGT in clinical practice for stroke survivors, overcoming the limited generalizability of the clinical randomised controlled trials. However, several limitations have to be taken into account. First, we cannot establish a direct cause-effect relationship between the analysed factors (RAGT dose, age and time since stroke); an amount of over ground walking physiotherapy-assisted walking was also performed during the multidisciplinary rehabilitation, even though RAGT was set as the primary treatment for gait restoration. Finally, the retrospective nature of the study limited the availability of the clinical data.

Conclusion

Patients with stroke (ischaemic and haemorrhagic) showed a similar level of functional recovery after a multidisciplinary rehabilitation that included a RAGT program. A higher dose of RAGT (>14 sessions), as well as a younger age (< 60 years old) and early rehabilitation (< 6 weeks since stroke) are determinant factors of favourable recovery. These findings need to be confirmed in prospective trials.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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